

CLAIMS

1. Human antibody having specificity for the activated C5 component of the complement system and characterised in that it inhibits the conversion of the C5 alpha chain to C5a and C5b.
- 5 2. Recombinant antibody according to claim 1 characterised in that it recognises an epitope comprising the proteolytic site for C5 convertase on the alpha chain of the C5 complement component.
3. Antibody according to claim 2 characterised in that it recognises a polypeptide having at least 80% homology with the peptide comprising the region
10 corresponding to sequence 731-740 of the C5 component of human complement, peptide having sequence KDMQLGR↓LHMKTLTPVSK (seq IDN 15).
4. Antibody according to claim 3 where in said C5 component is of mammalian origin, chosen among: human, mouse, rat, rabbit.
- 15 5. Antibody according to claims 1-4 characterised in that it is recombinantly produced.
6. Recombinant antibody according to claim 5, characterised in that it is in the form of single chain (scFv) comprising one variable region of the light chain covalently joined to one variable region of the heavy chain.
- 20 7. Antibody according to claim 6, characterised by the fact that the light chain is a lambda chain, preferably Vλ3/V2-14 or a kappa chain, preferably Vκ4/DPK24, and the variable region of the heavy chain is the VH3 region, preferably VH3/V-48.
8. Antibody according to claim 7, characterised in that it comprises at least one of
25 the amino acid sequences selected from the group consisting of: SEQ ID NO 2, 4, 6.
9. Recombinant antibody according to claim 8 characterised in that it has the amino acid sequence corresponding to SEQ ID NO 6.
10. Recombinant antibody according to claim 8 characterised in that it comprises
30 both the amino acid sequences identified as SEQ ID NO 2 and SEQ ID NO 4, or their allelic variants or their conservative mutations.

11. Recombinant antibody according to claim 5, characterised by the fact of comprising a polypeptide having at least 95% homology with at least one of the amino acid sequences corresponding to sequences SEQ ID NO 2, SEQ ID NO 4 or SEQ ID NO 6.
- 5 12. Recombinant antibody according to claim 8 characterised in that it comprises at least one of the sequences selected from the group consisting of seq IDN 2, 4 or 6 in combination with a sequence derived from an immunoglobulin heavy chain constant region.
- 10 13. Recombinant antibody according to claim 12 wherein said immunoglobulin heavy chain constant region is selected from the group consisting of: human Ig A heavy chain, human Ig G heavy chain, murine heavy gamma chain, rattus norvegicus heavy chain.
14. Recombinant antibody according to claim 13 characterised in that it is dimeric.
- 15 15. Recombinant chimeric protein characterised in that it comprises at least one of the sequences corresponding to sequences ID NO: 2, 4, 6, 8, 10, 12 or protein sequences having at least 95 % homology with said sequences.
16. Isolated nucleotide sequences encoding for antibodies according to claims 1-14.
- 20 17. Nucleotide sequences according to claim 15 characterised in that it comprises at least one of the sequences chosen among: SEQ ID NO 1 or 3 or 5, 7, 9, 11.
18. Vectors comprising nucleotide sequences according to claims 6 and 7.
19. Vectors according to claim 18 characterised by the fact of being expression vectors in bacteria, yeasts, or higher eukaryotic cells.
- 25 20. Antibodies according to claims 1-14 or proteins according to claim 15 for therapeutic or diagnostic use.
21. Nucleotide sequences according to claims 16-17 or vectors according to claims 17-18 for therapeutic or diagnostic use.
- 30 22. Use of antibodies or proteins according to claim 20 for pharmaceutical preparations for prevention and treatment of diseases involving hyperactivation of the complement system.

23. Use of the nucleotide sequences according to claim 21 for pharmaceutical preparation for treatment of diseases involving hyper-activation of the complement system.
24. Use according to claims 22 and 23 characterised in that these diseases are
5 due to hyper-production of Terminal C Complex.
25. Use according to claims 22 and 23 for the preparations of a medicament for chronic or acute inflammatory diseases.
26. Use according to claim 25 wherein the chronic disease is selected among:
rheumatoid arthritis, glomerulonephritis, multiple sclerosis, demyelinating
10 peripheral neuropathies, atherosclerosis.
27. Use according to claim 25 wherein the acute disease is selected among:
Multiple Organ Failure, myocardial infarction.
28. Use according to claim 25 for the preparation of a medicament for myocardium damage from reperfusion after ischaemia.
- 15 29. Pharmaceutical compositions comprising as the active principle anyone of the antibodies according to claims 1-14 or of the proteins according to claim 15 or of the nucleotide sequences according to claims 15-17 in combination with suitable excipients and/or diluents.
- 20 30. Process for selecting anti-C5 antibodies endowed with the ability of inhibiting the formation of C5a from C5, characterised in that it comprises a first selection step on C5 antigen and a second selection step by means of inhibition of hemolytic assay on SRBC.
31. Process for the preparation of the recombinant antibodies or proteins according to claims 1-5 characterised in that the isolated nucleotide
25 sequences according to claims 15-16 are used.
32. Use of antibodies according to claims 1-14 or of nucleotide sequences according to claims 16-17 for setting up animal models of diseases caused by hyper-activation of the complement system.
- 30 33. Kit comprising at least one of the antibodies according to claims 1-14 or at least one of the nucleotide sequences according to claims 16-17.

34. Process for the selection of inhibitors of the conversion of the C5 component of activated complement to its biologically active fragments, characterised by the use of antibodies or proteins according to claims 1-15.

35. Non-human transgenic animals, characterised by the fact of expressing
5 nucleotide sequences according to claims 13-17.

36. Isolated cells characterised by being transformed with the nucleotide
sequences according to claims 16-17 or by the vectors according to claims
18-19.

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